Amendments to the Specification

At page 1 of the specification, replace the paragraph under "Cross Reference to Earlier File Application" with the following amended paragraph:

This application is a division of U.S. Serial No. 09/122,126, filed July 24, 1998, now issued as U.S. Patent No. 6,451,575. This application claims the benefit of U.S. Provisional Application No. 60/053850 filed on July 25, 1997 and U.S. Provisional Application No. 60/055836 filed on August 15, 1997 and U.S. Provisional Application No. 60/062,169 (unknown at filing), filed on October 16, 1997.

At page 27 of the specification, replace the second complete paragraph which begins at line 15 with the following amended paragraph:

As used herein, the cleavage site "E272-374A" refers to the ITEGE373 (SEQ ID NO:49)-374ARGS (SEQ ID NO:50) bond of human aggrecan as well as to the homologous aggrecanase-sensitive cleavage site in aggrecan from various animal species, the cleavage site "E1545-1546G" refers to the SELE1545 (SEQ ID NO:51)-1546GRGT (SEQ ID NO:52) bond of human aggrecan as well as to the homologous aggrecanase-sensitive cleavage site in aggrecan from various animal species, the cleavage site "E1714-1715G" refers to the KEEE1714 (SEQ ID NO:53)-1715GLGS (SEQ ID NO:54) bond of the human aggrecan as well as to the homologous aggrecanase-sensitive cleavage site in aggrecan from various animal species, the cleavage site "E1819-1820L" refers to the TAQE1819 (SEQ ID NO:55)-1820AGEG (SEQ ID NO:56) bond of human aggrecan as well as to the homologous aggrecanase-sensitive cleavage site in aggrecan from various animal species, the cleavage site "E1919-1920L" refers to the ISQE1919 (SEQ ID NO:57)-1920LGQR (SEQ ID NO:58) bond of human aggrecan as well as to the homologous aggrecanase-sensitive cleavage site in aggrecan from various animal species.

At page 33 of the specification, replace the first complete paragraph which begins at line 14 with the following amended paragraph:

These aggrecan monomers (500 nM) were incubated at 37°C for at least 4 hr with ADMPs eluted from the Macro S support column in a final volume of 200 ul in Buffer B (Buffer B contains 50 nM Tris, pH 7.6, containing 0.1 M NaCl and 10 mM CaCl2), quenched with 20 mM EDTA and analyzed for aggrecan fragments produced exclusively by cleavage at the Glu^{373}-Ala^{374} bond within the aggrecan core protein using the monoclonal antibody, BC-3 (Hughes, C.E., et al., Biochem. J. 306:799-804, 1995). This antibody recognizes aggrecan fragments with the N-terminal sequence A^{374}RGSVIL... (SEQ ID NO:59), generated upon cleavage by ADMPs. The BC-3 antibody

recognizes this neoepitope only when it is in the N-terminus and not when it is present internally within aggrecan fragments or within the intact aggrecan core protein. Other proteases produced by cartilage in response to stimulation of chondrocytes do not cleave at the Glu^{373}-Ala^{374} site, therefore only products produced upon cleavage by ADMPs are detected.

At page 44 of the specification, replace the last complete paragraph which begins at line 24 and continues to page 45, line 10, with the following amended paragraph:

The peptide was linked to the carrier protein, keyhole limpet hemocyanin, and then subsequently used for immunization of a sheep. The coupled peptide antigen was suspended in PBS (phosphate-buffered saline) at 1 mg/ml with an equal volume of complete Freund's adjuvant. The material was mixed until it formed an emulsion, and then the material was injected at 6-8 subcutaneous sites. A total of 150-200 ug of coupled peptide was injected into the animal. The sheep was boosted every two weeks (for a total of five times) and a production bleed was collected at each time point. The affinity of the antibody was tested both in an ELISA and Western assay using the above antigen peptide conjugated to BSA. The polyclonal antiserum was positive for recognizing the BSA coupled peptide both in the ELISA and Western assays. The polyclonal sera was affinity purified over an antigen peptide (CASLSRFVETLVVADDK, SEQ ID NO:60) column to capture the high affinity IgG antibodies and remove the low affinity antibodies.